

REMARKS

Claim 1 has been amended to recite the reaction time of the enantioselective hydrogenation. Support for the amendment can be found, for example, at page 14, lines 15-16. No new matter has been added.

Rejections under 35 U.S.C §103

Claims 1-7, 10-14, 17 and 18 stand rejected under 35 USC §103 as allegedly being obvious over G. Helmchen et al.: (HOUBEB-WIEYL Methods of Organic Chemistry 4th Edition).

As the Examiner notes on page 3 of the Office Action, "Helmchen et al. fails to explicitly disclose the process where $n=1$, and the substitution of H or methyl on the ring structure of R1." The Examiner alleges: " that where $n=1$ this chemical change may be considered a first homologation, replacing the methyl groups with the ethyl group."

Contrary to the Examiner's allegations, the behavior of compounds where $n=0$ is different from compounds where $n=1$.

Compounds where $n=1$, such as formula I, are unstable substrates that eliminate amines easily, forming unwanted olefinic products. As mentioned on page 6 of the specification, the homogeneous hydrogenation of 3-aminoketones is regarded as problematical since in the majority of cases elimination products are obtained instead of the desired alcohol (J. Organomet. Chem. 1982, 232, C17 or Synlett, 1997, 1306). Surprisingly, in the process according to the invention, this elimination proves to be unimportant and the proportion of elimination product is less than 2%.

Because of the stability of compounds where $n=0$ (Helmchen et al.) this α , β -elimination reaction is not possible. Amines are not eliminated. As can be seen in table 6 of Helmchen et al. the addition of triethylamine is necessary for high yields. By contrast, in the present invention, amines would lead to a higher ratio of elimination product.

As discussed in the Examiner interview, the relevant compounds on table 6 of the Helmchen et al. reference, are based upon reference 40 (i.e., Hayashi et al: *Tetrahedron Letters* No. 5, 425-428), a copy of which is attached. As can be seen on page 426, line 2, hydrogenation of the relevant compounds was carried out in the presence of triethylamine and

BPPFOH-Rh⁺. Hydrogenation was complete in two to four days.

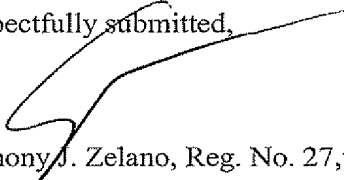
Furthermore, with regards to the surprisingly quick reaction time of the present invention (i.e., from 0.1 to 30 hours), as stated on page 428 of Hayashi et al., at post note 7, "In the absence of triethylamine, the hydrogenation is very slow." Thus, even in the presence of triethylamine the hydrogenation took 2-4 days to complete. In sharp contrast, in the present invention hydrogenation is complete, without the addition of triethylamines, in less than 30 hours.

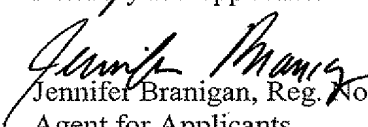
Surprisingly the process according to this invention results in the enantiomer of the end product with n=1 with high selectivity and yield without further transformations. Furthermore, the proportion of elimination product is less than 2% and the hydrogenation reaction takes place quickly. Thus, Applicants have shown that compounds where n=1 are not obvious homologs of compounds where n=0, as far as the claimed process is concerned.

Based on the above remarks it is respectfully requested that the rejection under 35 USC §103 be removed.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,


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